



PATENTS

Attorney Docket Number 102286.123

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Turski <i>et al.</i>	Art Unit:	1646
Serial No.:	09/746,662	Examiner:	Ruixiang Li
Filing Date:	December 22, 2000		
Title:	Treatment of Demyelinating Disorders		

Mail Stop ~~AP~~ *RCE (MD) 4/2/04*
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATION UNDER 37 C.F.R. § 1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed Mail Stop ~~AP~~, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

4/2/04
Date of Signature and
of Mail Deposit

RCE
(MD)
4/2/04

Maureen DiVito
Maureen DiVito

DECLARATION OF TERENCE SMITH UNDER 37 C.F.R. § 1.132

Dear Sir:

I, Terence Smith declare as follows:

1. I currently hold the position of Head of Pharmacology at Eisai London Research Laboratories Ltd., which is the assignee of the above-referenced patent application ("the Application"). I have worked, initially performing and latterly supervising, research in the field of multiple sclerosis, particularly animal models of the disease, since obtaining my Ph.D. in pharmacology in 1992. My professional experience, educational background, professional activities, and publications are

U.S.S.N. 09/746,662

detailed in the *curriculum vitae* attached hereto as Exhibit A. In addition, similar details are included for the co-inventor, Prof. Dr. Lechoslaw Turski, attached hereto as Exhibit B.

2. As one of the inventors, I have personal knowledge of the invention disclosed and claimed in the Application. I signed a previous Declaration dated August 28, 2003 addressing references cited against the Application.

3. It has been brought to my attention that, following submission of my previous Declaration, in an Advisory Action dated September 30, 2003, the Examiner maintained the rejection of claims 21-22 and 24-25 of the Application under 35 U.S.C. § 103(a) as allegedly being obvious over Shishikura *et al.*, U.S. Patent No. 6,133,258 ("Shishikura") in view of Csuzdi *et al.*, WO 97/28163 ("Csuzdi"), and the rejection of claims 23, 29-30, and 38 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Shishikura in view of Csuzdi and Prineas *et al.*, "Demyelinating Diseases," in Greenfield's Neuropathology, 813-896 (1997).

4. I reviewed the cited references and described my understanding regarding their teachings in my previous Declaration dated August 28, 2003. Below is a further explanation of my understanding of the teachings of the primary reference, Shishikura.

5. Shishikura deals with kainic acid neuronal excitotoxicity and protection against it. The reference describes pyridothiazine derivatives that provide potent inhibition of kainic acid neurotoxicity and anticonvulsant effect against seizure, and therefore are useful as agents for treating neurological disorders, including multiple sclerosis (*see, e.g.*, column 2, lines 39-59; column 15, lines 43-53).

6. Shishikura uses the effectiveness of pyridothiazine derivatives against seizures and against kainic acid excitotoxicity, which do not belong to the symptomatology of demyelinating disorders, as evidence for usefulness in the treatment of multiple sclerosis. Multiple sclerosis is included because its symptomatology includes spasticity (which is not necessarily associated with other demyelinating disorders), and AMPA antagonists were known to have muscle relaxant

U.S.S.N. 09/746,662

activity. Shishikura does not recognize that multiple sclerosis is a demyelinating disorder, and does not claim usefulness for therapy of such disorders.

7. Our Application is directed to the therapy of demyelination and the resulting cell death in demyelinating disorders, rather than direct neuroprotection against excitotoxicity induced by kainic acid or glutamate in neurological disorders as disclosed by Shishikura.

8. There is no known relationship between excitotoxicity and cell death due to demyelination. The mechanisms leading to demyelination are not known, and the literature does not teach that signs of excitotoxic cell death are seen in human tissue or tissue from animal models of demyelinating disorders (e.g., EAE models).

9. Therefore, it is NOT OBVIOUS that any compound which protects cells against excitotoxicity induced by kainic acid or against seizures as disclosed in Shishikura may be useful in therapy of demyelinating disorders, including multiple sclerosis. Notably, Shishikura does not mention demyelinating disorders, since at that time it was NOT OBVIOUS to the authors that the compounds claimed are useful for therapy of demyelinating disorders. Indeed, by using multiple sclerosis as an example of a neurological disorder and not using the term "demyelinating disorders" Shishikura itself provides evidence that it was not obvious for a person of ordinary skill in the art to suspect usefulness of AMPA antagonists in therapy of demyelinating disorders. Since it is NOT OBVIOUS that an action against seizures and kainic acid neurotoxicity can be useful in therapy of demyelinating disorders, Shishikura did not claim usefulness of pyridothiazine derivatives against demyelinating disorders.

10. In sum, it simply is NOT OBVIOUS that a person of ordinary skill in the art could conclude from Shishikura's disclosure of the usefulness of pyridothiazine derivatives in treatment of "Huntington's chorea, Parkinson's disease ... and multiple sclerosis" due to "inhibitory action against kainic acid neurotoxicity and anticonvulsant effect for ... seizure" (column 15, lines 43-53) that such agents are useful in therapy of demyelinating disorders.

U.S.S.N. 09/746,662

11. I have been informed that, in the Advisory Action dated September 30, 2003, the Examiner stated that the argument that Dr. Turski and I were the first to recognize the glutamate ionotropic AMPA receptor as a target for the treatment of demyelinating disorders is not persuasive because our work was published in Nature Medicine in 2000, which is after the prior art date of Shishikura. The Examiner's comment merely reemphasizes my statements above and in my previous Declaration. If the work described in our Application was first published in Nature Medicine in 2000, then Shishikura could not disclose or suggest the use of an AMPA receptor inhibitor for treating disorders induced by demyelination. The only teaching in Shishikura relates to the use of an AMPA receptor inhibitor for treating a neurological disorder caused by neurotoxicity. Information regarding the effect of the AMPA receptor on demyelination was only available after the prior art date of Shishikura, as acknowledged by the Examiner.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed: 
Terence Smith

Dated: 25th March 2004

CURRICULUM VITAE: TERENCE SMITH

EXHIBIT A

DATE OF BIRTH: 13th October 1964 **NATIONALITY:** British

ADDRESS (home): 4 The Old School, Norfolk Street, Cambridge, CB1 2LE UK
Telephone: 0044 (0)1223 323 524
e-mail: woodrow.smith@btopenworld.com

ADDRESS (work): Eisai London Research Laboratories Limited
Bernard Katz Building, University College London
Gower Street, London, WC1E 6BT UK
Telephone: 0044 (0)20 7413 1145
e-mail: Terence_Smith@eisai.net

CURRENT EMPLOYMENT

August 1997 – present:

Head of Pharmacology, Eisai London Research Laboratories, London.

In 1992 the London laboratories of Eisai, a leading Japanese pharmaceutical company, were established at UCL with the specific aim of developing novel therapies for CNS degenerative disease. I joined the company in 1997 to expand the portfolio of *in vivo* models of CNS disease. Under my guidance, models of the human demyelinating disease, multiple sclerosis (MS), were established and utilised in the drug screening process. During the past four years, a drug finding project, germinating from the exchange of ideas between London and Tsukuba (Japan), has flourished and now involves a score of researchers including chemists, cell biologists and pharmacologists. The fruition of this work was published in Nature Medicine (January 2000) and Phase I clinical studies were successfully completed September 2002. Phase IIa studies are currently on-going (completion anticipated Autumn 2003).

PREVIOUS EMPLOYMENT

October 1991 – July 1997:

Post Doctoral Research Scientist, Multiple Sclerosis Laboratory, Institute of Neurology, 1 Wakefield Street, London WC1N 1PJ.

October 1990 - September 1991

Research Assistant. Department of Medicine, Charing Cross and Westminster Medical School, St. Dunstan's Road, Hammersmith, London, W6 8RP.

October 1987 - September 1990

Ph.D Student (MRC Funded). Department of Pharmacology, Charing Cross and Westminster Medical School, St. Dunstan's Road, Hammersmith, London, W6 8RP.

August 1985 - July 1986

Sandwich Student. Applied Physiology Division, Institute of Naval Medicine, Alverstoke, Hampshire. Lung function laboratory operator; thermal and exercise physiology studies on naval ratings.

ACADEMIC QUALIFICATIONS

January 1992: Ph.D. Faculty of Science, University of London

Thesis entitled "The Influence of Glucocorticoids on the Expression of Lipocortins 1,2 and 5 in the Brain and Pituitary Gland of the Rat

July 1987: B.Sc. Honours Degree in Applied Biological Sciences (Upper Second Class)
University of the West of England (formerly Bristol Polytechnic)

1983 Four 'A' Levels

1978 Eight 'O' Levels

INVITED TALKS

Open University, 5 May 2003, Milton Keynes, UK.

Symposium: Relevance of cell death in development and disease of the brain. Charité Hospital, Humboldt University 24-25 February 2003, Berlin, Germany.

Cambridge University Department of Neurology, 10 December 2002, Cambridge, UK.

3rd European School of Neuroimmunology, 11-14 September 2002, Tampere, Finland.

British Inflammation Research Association 3-4 July 2002, Bath, UK.

Euroglia 21-25 May 2002, Rome, Italy.

PUBLICATIONS

Groom A.J., **Smith T.**, Turski L. (2003). Multiple sclerosis and glutamate. *Ann N Y Acad Sci.* 993:229-75; discussion 287-8.

Ohgoh M., Hanada T., **Smith T.**, Hashimoto T., Ueno M., Yamanishi Y., Watanabe M. and Nishizawa Y. (2002). Altered expression of glutamate transporters in experimental autoimmune encephalomyelitis. *J. Neuroimmunol.* 125: 170-178.

Banati R.B., Newcombe J., Gunn R.N., Cagnin A., Turkheimer F., Heppner F., Price G., Wegner F., Giovannoni G., Miller D.H., Perkin G.D., **Smith T.**, Hewson A.K., Bydder G., Kreutzberg G.W., Jones T., Cuzner M.L. and Myers R. (2000). The peripheral benzodiazepine binding site in the brain in multiple sclerosis: quantitative in vivo imaging of microglia as a measure of disease activity. *Brain* 123:2321-2337.

Smith T., Groom A., Zhu B. and Turski L. (2000). Autoimmune encephalomyelitis ameliorated by AMPA antagonists. *Nature Medicine* 6: 62-66.

Folcik V.A., **Smith T.**, O'Bryant S., Kawczak J.A., Zhu B., Sakuri H., Kajiwar A., Staddon J.M., Glabinski A., Chernosky A.L. Tani M., Johnson J.M., Tuohy V.K., Rubin L.L. and Ransohoff R.M. (1999). Treatment with BBB022A or rolipram stabilizes the blood-brain barrier in experimental autoimmune encephalomyelitis: an additional mechanism for the therapeutic effect of type IV phosphodiesterase inhibitors. *J. Neuroimmunol.* 97: 119-128.

Smith T., Hewson A.K., Kingsley C.I., Leonard J.P. and Cuzner M.L. (1997). Interleukin-12 induces relapses in experimental allergic encephalomyelitis in the Lewis rat. *Am. J. Pathol.* 150: 1909-1917.

Leonard J.P., Waldburger K.E., Schaub R.G., **Smith T.**, Hewson A.K., Cuzner M.L. and Goldman S.J. (1997). Regulation of the inflammatory response in animal models of multiple sclerosis by interleukin-12. *Crit. Rev. Immunol.* 17: 545-553.

Smith T., Schmeid M., Hewson A.K., Lassmann H. and Cuzner M.L. (1996). Apoptosis of T-cells and macrophages in the central nervous system of intact and adrenalectomised Lewis rats during experimental allergic encephalomyelitis. *J. Autoimmun.* 9: 167-174.

Storch M.K., Fischer-Colbrie R., **Smith T.**, Rinner W.A., Hickey W.F., Cuzner M.L., Winkler H and Lassmann H. (1996). Co-localization of secretoneurin immunoreactivity and macrophage infiltration in the lesions of experimental autoimmune encephalomyelitis. *Neuroscience* 71:885-893.

Hewson A.K., **Smith T.** and Cuzner, M.L. (1995). Suppression of experimental allergic encephalomyelitis in the Lewis rat by the matrix metalloprotease inhibitor Ro31-9790. *Inflamm. Res.* 44:345-349.

Smith S.F., Benjamin J., Dewar A., Sheppard M., Fox B., **Smith T.**, Guz A. and Tetley T.D. (1995). Effect of dexamethasone on carrageenin-induced inflammation in the lung. *Med. Inflamm.* 4: 273-281.

Smith S.F., Tetley T.D., Datta A.K., **Smith T.**, Guz A. and Flower R.J. (1995). Lipocortin-1 distribution in bronchoalveolar lavage from healthy human lung: effect of prednisolone. *J. Appl. Physiol.* 79: 121-128.

Smith T., Hewson A.K., Quarrie L., Leonard J.P. and Cuzner M.L. (1994). Hypothalamic PGE₂ and cAMP production and adrenocortical activation following intra-peritoneal endotoxin injection: *in vivo* microdialysis studies in Lewis and Fischer rats. *Neuroendocrinol.* 59: 396-405.

Smith T. and Cuzner M.L. (1994). Neuroendocrine-immune interactions in homeostasis and autoimmunity. *Neuropathol. Appl. Neurobiol.* 20: 413-422.

Smith T., Flower R.J. and Buckingham J.C. (1993). Lipocortins 1,2 and 5 in the central nervous system and pituitary gland of the rat: selective induction by dexamethasone of lipocortin 1 in the anterior pituitary gland. *Mol. Neuropharmacol.* 3: 45-55.

Invited book chapters

Smith T. and Hewson A.K. (1997). Neuroendocrine-induced immune modulation and autoimmunity. In the *Handbook of Immune Modulating Agents*. Editor Kresina, T.F. pp 363-383. Marcell Dekker Inc. NY.

Cuzner M.L. and **Smith T.** (1995). Immune responses in the central nervous system in inflammatory demyelinating disease: in *Immune Responses in the Nervous System. The Molecular and Cellular Neurobiology Series*. Editor Rothwell, N.J. pp 117-142. Bios Scientific Publishers.

Buckingham J.C., **Smith T.** and Loxley H.D. (1991). The control of ACTH Secretion: in *The Adrenal Gland (second edition). Comprehensive Endocrinology (revised series)*. Editor James, V.H.T. pp. 131-158. London: Raven Press.

CURRICULUM VITAE

Name: Prof. Dr. med. LA Turski MD

Date and place of birth: August 10, 1955, Opole-Lubelskie, Poland

Marital status: Married to Prof. Dr. med. C Ikonomidou, MD
(Greek/German) since October 12, 1985

Nationality: German

Children: Christopher Andreas Turski (December 3, 1986)
Gabrielle Nicole Turski (April 25, 1990)
Jennifer Sabrina Turski (June 22, 2000)

Business address: Solvay Pharmaceuticals bv
C.J. van Houtenlaan 36
NL-1381 CP Weesp
The Netherlands
E-mail: Les.Turski@solvay.com; LTurski@aol.com

Home address: Prof. Dr. med. L. Turski
Jörsstr. 16
D-13505 Berlin

Education:

Primary school

1961-1969: Primary school No. 2 in Opole-Lubelskie, Poland

Secondary school

1969-1972: Adam-Mickiewicz Gymnasium in Opole-Lubelskie,
Poland

Graduate school

1972-1978: Lublin Medical School, Poland

1980: MD Lublin Medical School, Poland
Thesis title: Central action of kainic acid in rats

1988: PhD Georg-August-University Göttingen, Germany
Thesis title: The convulsant action of pilocarpine in
rats: Pharmacological, electroencephalographic and
morphological
analysis of the role of cholinergic mechanisms in
epileptogenesis

Clinical training:

1978-1981: Resident, Internal Medicine, Department of Internal Medicine, Lublin Medical School, Poland

Management training:

1997: University of Michigan Business School, Ann Arbor, MI, USA

Licensure and certifications:

1978: Polish Medical Licence
 1993: German Medical Licence (22.09.1993)
 1994: German Board of Pharmacology and Toxicology
 1997: German Board of Clinical Pharmacology

Positions held:

1978-1981: Resident in Pharmacology and Toxicology at the Institute of Clinical Pathology, Department of Pharmacology, Lublin Medical School, Poland

1978-1981: Resident in Internal Medicine at the Institute of Internal Medicine, Department of Gastroenterology, Lublin Medical School, Poland

1981-1983: Postdoctoral Fellow with K Kuschinsky MD, Department of Biochemical Pharmacology, Max-Planck-Institute for Experimental Medicine, Göttingen, Germany

1983-1984: Postdoctoral Fellow with K-H Sontag PhD, Max-Planck-Institute for Experimental Medicine, Göttingen, Germany

1984: Postdoctoral Fellow with BS Meldrum MD, Department of Neurology, Institute of Psychiatry, University of London, London SE5 8AF, UK

1985-1987: Assistant Professor, Max-Planck-Institute for Experimental Medicine, Göttingen, Germany

1984-1988: Assistant Professor of Pharmacology, Department of Pharmacology, Institute of Clinical Pathology, Lublin Medical School, Poland

1988-1993: Associate Professor of Neuropharmacology, Department of Pharmacology and Toxicology, Georg-August-University, Göttingen, Germany

1993- Professor of Pharmacology, Department of Pharmacology and Toxicology, Georg-August-University, Göttingen, Germany

1987-1997: Head of Experimental Neurology, Research

1997-1999:	Laboratories of Schering AG, Berlin, Germany Director of Pharmacology, University College London,
1999-2001:	Eisai London Research Laboratories, London, UK Head of Research, Solvay Pharmaceuticals bv, Weesp, The Netherlands
2001-	Vice President Global Discovery, Solvay Pharmaceuticals bv, Weesp, The Netherlands and Solvay Pharmaceuticals GmbH, Hannover, Germany

Fellowships and scholarships:

1. Fellowship - European Training Programme in Brain and
Behaviour Research - France (Strasbourg) - 1981
2. Fellowship - Max-Planck-Society Fellowship for Visiting
Scientists, 1981-1983

Memberships in professional societies:

German Society of Pharmacology and Toxicology
International Basal Ganglia Society
Society for Neuroscience

Honors and awards:

1972	Scapula aurea awarded by the Lublin Medical School
1977	Award of the Student Scientific Association, Poznan Medical School, Poland
1978	Award of the Student Scientific Association, Katowice, Silesian Medical School, Poland
1983	Award of the Minister of Health and Public Care for Research Achievements, Warsaw, Poland (1st Prize)
1984	1st Prize of the Polish Academy of Sciences, Warsaw, Poland
1985-1986	Michael Prize for Epilepsy Research, Jerusalem, Israel

L Turski

PUBLICATIONS

Department of Pharmacology
Institute of Clinical
Pathology
Medical School
Jaczewskiego 8
PL-20090 Lublin
Poland

Department of Biochemical
Pharmacology
Max-Planck Institute
for Experimental Medicine
Hermann-Rein Str. 3
D-37075 Göttingen
Germany

Department of Neuropsychopharmacology
Research Laboratories
of Schering AG
Müllerstr. 178
D-13342 Berlin
Germany

Department of Pharmacology
Eisai London
Research Laboratories
University College London
Gower Street
London WC1E 6BT
UK

Solvay Pharmaceuticals bv
Solvay Pharmaceuticals Research Laboratories
C.J. van Houtenlaan 36
NL-1381 CP Weesp
The Netherlands

1. Rechberger T, Turski L, Turski W, Wojcik E (1979) The influence of atropine on the antiamphetamine action of fluphenazine. *Ann Univ M Curie-Sklodowska (Lublin) Sectio D* 34: 333-339
2. Kleinrok Z, Czuczwar SJ, Turski L (1980) Prevention of kainic acid-induced seizure-like activity by antiepileptic drugs. *Pol J Pharmacol Pharm* 32: 261-264
3. Kleinrok Z, Czuczwar SJ, Turski L, Zarkowski A (1980) Effect of intracerebroventricular injection of kainic acid on electrically and chemically induced convulsions in mice. *Pol J Pharmacol Pharm* 32: 265-269
4. Kleinrok Z, Turski L, Wawrzyniak M, Cybulska R (1980) The locomotor and exploratory activities in rats after lesion of hippocampal pyramidal cells with kainic acid. *Pol J Pharmacol Pharm* 32: 625-637
5. Kleinrok Z, Turski L (1980) Kainic acid-induced wet dog shakes in rats. The relation to central neurotransmitters. *Naunyn-Schmiedeberg's Arch Pharmacol* 314: 37-46
6. Turski L, Kleinrok Z (1980) Effects of kainic acid on body temperature of rats. Role of catecholaminergic and serotonergic systems. *Psychopharmacology* 71: 35-39
7. Turski L, Turski W, Czuczwar SJ, Kleinrok Z (1981) Effects of morphine and nalorphine on kainic acid-induced hypothermia in rats. *Psychopharmacology* 72: 211-214
8. Czuczwar SJ, Turski L, Kleinrok Z (1981) Atropine reversal of kainic acid-induced decrease in the leptazol convulsive threshold. *J Pharm Pharmacol* 33: 44-45
9. Kleinrok Z, Turski L, Wawrzyniak M, Cybulska R (1981) The locomotor and stereotypy response to dopaminergic drugs and caffeine after intracerebroventricular kainic acid in rats. *Pol J Pharmacol Pharm* 33: 149-159
10. Kleinrok Z, Turski L (1981) Biochemical consequences of kainic acid injection into the lateral brain ventricle in rat. *Acta Bioch Pol* 28: 111-122
11. Czuczwar SJ, Turski L, Turski W, Kleinrok Z (1981) Effects of some antiepileptic drugs in pentylenetetrazol-induced convulsions in mice lesioned with kainic acid. *Epilepsia* 22: 407-414
12. Czuczwar SJ, Turski L, Kleinrok Z (1981) Diphenylhydantoin potentiates the protective effect of diazepam against pentylenetetrazol but not against bicuculline and isoniazid-induced seizures in mice. *Neuropharmacology* 20: 675-679
13. Czuczwar SJ, Turski L, Turski W, Kleinrok Z (1981) Effect of combined treatment of phenytoin with diazepam on the susceptibility of mice to electroconvulsions. *J Pharm Pharmacol* 33: 672-673
14. Turski L, Czuczwar SJ, Turski W, Kleinrok Z (1981) Studies of carbachol-induced wet-dog shake behaviour in rats. *Psychopharmacology* 73: 81-83
15. Turski L, Turski W, Czuczwar SJ, Kleinrok Z (1981) Evidence against the involvement of serotonergic mechanisms in wet dog shake behaviour induced by carbachol chloride in rats. *Psychopharmacology* 73: 376-380

16. Turski L, Czuczwar SJ, Turski W, Kleinrok Z (1981) Effect of antidepressant drugs on carbachol chloride-induced wet dog shake behaviour in rats. *Neuropharmacology* 20: 1193-1196
17. Turski L, Czuczwar SJ, Turski W, Kleinrok Z (1981) Effect of trazodone, mianserin, iprindole and zimelidine on wet dog shakes produced by carbachol in rats. *J Pharm Pharmacol* 33: 670-671
18. Turski L, Czuczwar SJ, Turski W, Kleinrok Z (1981) Shuttle behaviour in rats after lesion of hippocampal pyramidal cells with kainic acid. *Meth Find Exptl Clin Pharmacol* 3: 361-366
19. Turski W, Turski L, Czuczwar SJ, Kleinrok Z (1981) (RS)- α -Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid: Wet dog shakes, catalepsy and body temperature changes in rats. *Pharm Bioch Behav* 15: 546-549
20. Czuczwar SJ, Turski L, Kleinrok Z (1981) Effects of morphine, nalorphine and morphine withdrawal on lethal toxicity of intracerebroventricular kainic acid in mice. *Pol J Pharmacol Pharm* 33: 611-614
21. Turski L, Czuczwar SJ, Turski W, Kleinrok Z (1982) Induction of wet dog shakes by intracerebroventricular bethanechol in rats. Antagonism by neurotransmitter receptor blockers. *Pharmacology* 24: 105-110
22. Turski W, Czuczwar SJ, Turski L, Kleinrok Z (1982) The involvement of catecholaminergic mechanisms in the appearance of wet dog shakes produced by carbachol chloride in rats. *Arch int Pharmacodyn Ther* 255: 204-211
23. Turski L, Czuczwar SJ, Turski W, Sieklucka-Dziuba M, Kleinrok Z (1982) Diphenylhydantoin enhancement of diazepam effects on locomotor activity in mice. *Psycharmacology* 76: 198-200
24. Czuczwar SJ, Turski L, Kleinrok Z (1982) Effects of combined treatment with diphenylhydantoin and different benzodiazepines on pentylenetetrazol- and bicuculline-induced seizures in mice. *Neuropharmacology* 21: 563-567
25. Turski W, Czuczwar SJ, Turski L, Kleinrok Z (1982) Bilateral injection of kainic acid into the rat striatum potentiates morphine, arecoline and pilocarpine but not haloperidol catalepsy. *Meth Find Exptl Clin Pharmacol* 4: 287-291
26. Czuczwar SJ, Turski L, Turski W, Kleinrok Z (1982) Convulsant action of pentetrazol in rats with selective lesions of the hippocampal pyramidal cells with intracerebroventricular kainic acid. *Meth Find Exptl Clin Pharmacol* 4: 293-298
27. Turski L, Havemann U, Kuschinsky K (1982) Evidence for functional interactions of morphine in substantia nigra and striatum, in relation to muscular rigidity in rats. *Neurosci Lett* 28: 291-296
28. Turski L, Havemann U, Kuschinsky K (1982) Evidence that opioid receptors in the substantia nigra pars reticulata are relevant in regulating the function of striatal efferent pathways. *Behav Brain Res* 5: 415-422

29. Havemann U, Turski L, Kuschinsky K (1982) Role of gabaergic mechanisms in the substantia nigra pars reticulata in modulating morphine-induced muscular rigidity in rats. *Neurosci Lett* 31: 25-30
30. Turski W, Czuczwar SJ, Turski L, Kleinrok Z (1982) Effect of glutamic acid diethylester on (RS)- α -amino-3-hydroxy-5-ethyl-4-isoxazolepropionic acid- and kainic acid-induced changes of body temperature in rats. *Pol J Pharmacol Pharm* 34: 161-167
31. Czuczwar SJ, Turski L, Kleinrok Z (1982) Anticonvulsant action of phenobarbital, diazepam, carbamazepine, and diphenylhydantoin in the electroshock test in mice after lesion of hippocampal pyramidal cells with intracerebroventricular kainic acid. *Epilepsia* 23: 377-382
32. Havemann U, Turski L, Kuschinsky K (1982) Role of opioid receptors in the substantia nigra in morphine-induced muscular rigidity. *Life Sci* 31: 2319-2322
33. Turski L, Havemann U, Schwarz M, Kuschinsky K (1982) Disinhibition of nigral GABA output neurons mediates muscular rigidity elicited by striatal opioid receptor stimulation. *Life Sci* 31: 2327-2330
34. Turski L, Havemann U, Kuschinsky K (1982) On the possible role of excitatory amino acids in the striatum in mediating morphine-induced muscular rigidity. *Pharm Bioch Behav* 17: 715-719
35. Turski L, Schwarz M, Sontag K-H (1982) Interaction between phenytoin and diazepam in mutant Han-Wistar rats with progressive spastic paresis. *Naunyn-Schmiedeberg's Arch Pharmacol* 321: 48-51
36. Czuczwar SJ, Turski L, Kleinrok Z (1982) Diphenylhydantoin-induced potentiation of the anticonvulsant effect of diazepam against some types of experimental seizures. *Wiss Zeit Humboldt Univ (Berlin) Math-Nat R* 31: 493-494
37. Kleinrok Z, Turski L, Czuczwar SJ, Turski W (1982) Carbachol-induced wet dog shakes - A model for studying antidepressant drugs? *Wiss Zeit Humboldt Univ (Berlin) Math-Nat R* 31: 519-521
38. Turski WA, Cavalheiro EA, Turski L, Kleinrok Z (1983) Intrahippocampal bethanechol in rats: Behavioural, electroencephalographic and neuropathological correlates. *Behav Brain Res* 7: 361-370
39. Schwarz M, Turski L, Janiszewski W, Sontag K-H (1983) Is the muscle relaxant effect of diazepam in spastic mutant rats mediated through GABA-independent benzodiazepine receptors? *Neurosci Lett* 36: 175-180
40. Turski L, Havemann U, Kuschinsky K (1983) The role of the substantia nigra in motility of the rat. Muscular rigidity, body asymmetry and catalepsy after injection of morphine into the nigra. *Neuropharmacology* 22: 1039-1048
41. Schwarz M, Turski L, Sontag K-H (1983) Reversal of the muscle relaxant effect of diazepam but not of progabide by a specific benzodiazepine antagonist: Ro 15-1788. *Eur J Pharmacol* 90: 139-142

42. Turski WA, Czuczwar SJ, Kleinrok Z, Turski L (1983) Does morphine withdrawal produce brain damage in rats? *Life Sci* 33: S397-S400
43. Turski WA, Czuczwar SJ, Kleinrok Z, Schwarz M, Turski L (1983) Intraamygdaloid morphine produces seizures and brain damage in rats. *Life Sci* 33: S615-S618
44. Turski L, Havemann U, Kuschinsky K (1983) Reversal of the muscle relaxant effect of diazepam by the specific benzodiazepine antagonist Ro 15-1788: An electromyographic study in morphine model of muscular rigidity in rats. *Life Sci* 33: S755-S758
45. Havemann U, Turski L, Schwarz M, Kuschinsky K (1983) Nigral GABAergic mechanisms and EMG activity in rats: Differences between pars reticulata and pars compacta. *Eur J Pharmacol* 92: 49-56
46. Turski WA, Cavaleiro EA, Schwarz M, Czuczwar SJ, Kleinrok Z, Turski L (1983) Limbic seizures produced by pilocarpine in rats: A behavioural, electroencephalographic and neuropathological study. *Behav Brain Res* 9: 315-335
47. Turski WA, Czuczwar SJ, Kleinrok Z, Turski L (1983) Cholinomimetics produce seizures and brain damage in rats. *Experientia* 39: 1408-1411
48. Turski WA, Czuczwar SJ, Turski L, Sieklucka-Dziuba M, Kleinrok Z (1984) Studies on the mechanism of wet dog shakes produced by carbachol in rats. *Pharmacology* 28: 112-120
49. Turski WA, Schwarz M, Turski L, Sontag K-H (1984) A specific benzodiazepine antagonist CGS 8216 reverses the muscle relaxant effect of diazepam but not that of phenobarbitone. *Eur J Pharmacol* 98: 441-444
50. Czuczwar SJ, Turski L, Schwarz M, Turski WA, Kleinrok Z (1984) Effects of excitatory amino acid antagonists on the anticonvulsant action of phenobarbital or diphenylhydantoin in mice. *Eur J Pharmacol* 100: 357-362
51. Turski L, Schwarz M, Sontag K-H (1984) Stereotypy, locomotor and cataleptic effects produced by drugs influencing dopaminergic systems in a mutant strain of Wistar rats: A genuine model of basal ganglia dysfunction? *Behav Brain Res* 12: 29-37
52. Turski L, Havemann U, Kuschinsky K (1984) Role of muscarinic cholinergic mechanisms in the substantia nigra pars reticulata in mediating muscular rigidity in rats. *Naunyn-Schmiedeberg's Arch Pharmacol* 327: 14-17
53. Schwarz M, Turski L, Sontag K-H (1984) CGS 8216, Ro 15-1788 and methyl- β -carboline-3-carboxylate, but not EMD 41717 antagonize the muscle relaxant effect of diazepam in genetically spastic rats. *Life Sci* 35: 1445-1451
54. Turski L, Schwarz M, Turski WA, Ikonomidou C, Sontag K-H (1984) Effect of aminophylline on muscle relaxant action of diazepam and phenobarbitone in genetically spastic rats: Further evidence for a purinergic mechanism in the action of diazepam. *Eur J Pharmacol* 103: 99-105

55. Turski WA, Cavalheiro EA, Bortolotto ZA, Mello LM, Schwarz M, Turski L (1984) Seizures produced by pilocarpine in mice: A behavioural, electroencephalographic and morphological analysis. *Brain Res* 321: 237-253
56. Turski L, Havemann U, Kuschinsky K (1984) GABAergic mechanisms in mediating muscular rigidity, catalepsy and postural asymmetry in rats: Differences between dorsal and ventral striatum. *Brain Res* 322: 49-57
57. Turski WA, Cavalheiro EA, Calderazzo-Filho LS, Kleinrok Z, Czuczwar SJ, Turski L (1985) Injections of picrotoxin and bicuculline into the amygdaloid complex of the rat: An electroencephalographic, behavioural and morphological analysis. *Neuroscience* 14: 37-53
58. Turski L, Schwarz M, Turski WA, Klockgether T, Sontag K-H, Collins JF (1985) Muscle relaxant action of excitatory amino acid antagonists. *Neurosci Lett* 53: 321-326
59. Turski L, Ikonomidou C, Cavalheiro EA, Kleinrok Z, Czuczwar SJ, Turski WA (1985) Effects of morphine and naloxone on pilocarpine-induced convulsions in rats. *Neuropeptides* 5: 315-318
60. Klockgether T, Schwarz M, Turski L, Wolfarth S, Sontag K-H (1985) Rigidity and catalepsy after injections of muscimol into the ventromedial thalamic nucleus: An electromyographic study in the rat. *Exp Brain Res* 58: 559-569
61. Klockgether T, Schwarz M, Turski L, Sontag K-H (1985) ZK 91296: An anticonvulsant β -carboline which lacks muscle relaxant properties. *Eur J Pharmacol* 110: 309-315
62. Turski L, Schwarz M, Turski WA, Sontag K-H (1985) Muscle relaxant action of 2-chloroadenosine in genetically spastic rats is independent of γ -aminobutyric acid-mediated inhibition. *Neurosci Lett* 54: 369-374
63. Chapman AG, Hart GP, Meldrum BS, Turski L, Watkins JC (1985) Anticonvulsant activity of two novel piperazine derivatives with potent kainate antagonist activity. *Neurosci Lett* 55: 325-330
64. Turski L, Meldrum BS, Jones AW, Watkins JC (1985) Anticonvulsant action of stereoisomers of γ -glutamylaminomethylsulphonic acid in mice. *Eur J Pharmacol* 113: 279-283
65. Turski L, Meldrum BS, Collins JF (1985) Anticonvulsant action of β -kainic acid in mice. Is β -kainic acid an N-methyl-D-aspartate antagonist? *Brain Res* 336: 162-166
66. Ikonomidou C, Turski L, Klockgether T, Schwarz M, Sontag K-H (1985) Effects of methyl β -carboline-3-carboxylate, Ro 151788 and CGS 8216 on muscle tone in genetically spastic rats. *Eur J Pharmacol* 113: 205-213
67. Bortolotto ZA, Mello LEM, Turski L, Cavalheiro EA (1985) Effects of 2-chloroadenosine on amygdaloid and hippocampal kindled seizures. *Arch Int Pharmacodyn Ther* 277: 313-330
68. Czuczwar SJ, EA Cavalheiro, Turski L, Turski WA, Kleinrok Z (1985) Phosphonic analogues of excitatory amino acids raise the threshold for maximal electroconvulsions in mice. *Neurosci Res* 3: 86-90

69. Czuczwar SJ, Turski L, Chmielewska B, Turski WA, Kleinrok Z (1985) Modification of the anticonvulsant activity of 2-amino-5-phosphonovalerate by agents affecting different neurotransmitter systems. *Neuropharmacology* 24: 965-968
70. Turski L, Schwarz M, Cavalheiro EA, Turski WA, Ikonomidou C, Sontag K-H (1985) Nigral GABAergic mechanisms modify the development of seizures produced by pilocarpine in rats: Behavioural, electroencephalographic and neuroanatomical evidence. *J cereb Blood Flow Metab* 5: S363-S364
71. Turski L, Schwarz M, Golembiowska-Nikitin K, Osborne NN, Klockgether T, Sontag K-H (1985) Intrastriatal bethanechol in rats: Seizures and brain damage. *J cereb Blood Flow Metab* 5: S361-S362
72. Klockgether T, Pardowitz I, Schwarz M, Sontag K-H, Turski L (1985) Evaluation of the muscle relaxant properties of a novel β -carboline, ZK 93423 in rats and cats. *Brit J Pharmacol* 86: 357-366
73. Czuczwar SJ, Turski WA, Ikonomidou C, Turski L (1985) Aminophylline and CGS 8216 reverse the protective action of diazepam against electroconvulsions in mice. *Epilepsia* 26: 693-696
74. Schwarz M, Lbscher W, Turski L, Sontag K-H (1985) Disturbed GABAergic transmission in mutant Han-Wistar rats: Further evidence for the basal ganglia dysfunction. *Brain Res* 347: 258-267
75. Turski WA, Cavalheiro EA, Ikonomidou C, Mello LEAM, Bortolotto ZA, Turski L (1985) Effects of aminophylline and 2-chloroadenosine on seizures produced by pilocarpine in rats: Morphological and electroencephalographic correlates. *Brain Res* 361: 309-323
76. Meldrum BS, Turski L, Schwarz M, Czuczwar SJ, Sontag K-H (1986) Anticonvulsant action of 1,3-dimethyl-5-aminoadamantane. Pharmacological studies in rodents and baboon, Papio Papiu. *Naunyn-Schmiedeberg's Arch Pharmacol* 332: 93-97
77. Czuczwar SJ, Ikonomidou C, Kleinrok Z, Turski L, Turski WA (1986) Effect of aminophylline upon the protective action of common antiepileptic drugs against electroconvulsions in mice. *Epilepsia* 27: 204-208
78. Ikonomidou C, Schwarz M, Turski L, Sontag K-H (1986) Muscle relaxant action of phenobarbitone in genetically spastic rats: An electromyographic study. *Eur J Pharmacol* 128: 1-7
79. Ellenbroek B, Klockgether T, Turski L, Schwarz M (1986) Distinct sites of functional interaction between dopamine, acetylcholine and GABA within the neostriatum: An electromyographic study in rats. *Neuroscience* 17: 79-88
80. Turski L, Cavalheiro EA, Schwarz M, Turski WA, de Moraes Mello LEA, Bortolotto ZA, Klockgether T, Sontag K-H (1986) Susceptibility to seizures produced by pilocarpine in rats after microinjection of isoniazid and γ -vinyl-GABA into the substantia nigra. *Brain Res* 372: 294-309

81. Turski L, Cavalheiro EA, Schwarz M, Turski WA, de Moraes Mello LEA, Bortolotto ZA, Klockgether T, Sontag K-H (1986) Susceptibility to seizures produced by pilocarpine in rats after microinjection of isoniazid or γ -vinyl-GABA into the substantia nigra. *Epilepsy Adv Clin Exp Res* 1: 3-4
82. Schwarz M, Ikonomidou C, Klockgether T, Turski L, Ellenbroek B, Sontag K-H (1986) The role of striatal cholinergic mechanisms for the development of limb rigidity: An electromyographic study in rats. *Brain Res* 373: 365-372
83. Turski L, Cavalheiro EA, Turski WA, Meldrum BS (1986) Excitatory neurotransmission within substantia nigra pars reticulata regulates threshold for seizures produced by pilocarpine in rats: Effects of intranigral 2-amino-7-phosphonoheptanoate and N-methyl-D-aspartate. *Neuroscience* 18: 61-77
84. Klockgether T, Schwarz M, Turski L, Sontag K-H (1986) The rat ventromedial thalamic nucleus and motor control: Role of N-methyl-D-aspartate mediated excitation, GABAergic inhibition and muscarinic transmission. *J Neurosci* 6: 1702-1711
85. Cavalheiro EA, Turski L (1986) Intrastriatal N-methyl-D-aspartate prevents amygdala kindled seizures in rats. *Brain Res* 377: 173-176
86. Turski L, Schwarz M, Klockgether T, Sontag K-H (1986) Substantia nigra and entopeduncular nucleus: Supraspinal sites of muscle relaxant action of tizanidine. *Brain Res* 379: 367-371
87. Turski L, Cavalheiro EA, Sieklucka-Dziuba M, Ikonomidou C, Czuczwar SJ, Turski WA (1986) Seizures produced by pilocarpine: Neuropathological sequelae and activity of glutamate decarboxylase in the rat forebrain. *Brain Res* 398: 37-48
88. Klockgether T, Turski L, Schwarz M, Sontag K-H (1986) Motor actions of excitatory amino acids and their antagonists within the rat ventromedial thalamic nucleus. *Brain Res* 399: 1-9
89. Ikonomidou C, Cavalheiro EA, Turski WA, Bortolotto ZA, Turski L (1987) Convulsant action of morphine, [D-Ala², D-Leu⁵]-enkephalin and naloxone in the rat amygdala: electroencephalographic, morphological and behavioural sequelae. *Neuroscience* 20: 669-684
90. Turski L, Klockgether T, Schwarz M, Sontag K-H, Meldrum BS (1987) Unusual interactions of excitatory amino acid receptor agonists: α - and β -kainate antagonise motor responses to N-methyl-D-aspartate in rodents. *Neuroscience* 20: 285-292
91. Turski L, Meldrum BS, Cavalheiro EA, Calderazzo-Filho LS, Bortolotto ZA, Ikonomidou C, Turski WA (1987) Paradoxical anticonvulsant activity of the excitatory amino acid, N-methyl-D-aspartate, in the rat caudate-putamen. *Proc Natl Acad Sci USA* 84: 1689-1693
92. Turski L, Klockgether T, Sontag K-H, Herrling PL, Watkins JC (1987) Muscle relaxant and anticonvulsant activity of 3-((+)-2-carboxy-piperazin-4-yl)-propyl-1-phosphonic acid, a novel N-methyl-D-aspartate antagonist, in rodents. *Neurosci Lett* 73: 143-148

93. Czuczwar SJ, Kleinrok Z, Turski L, Turski WA (1987) Effect of aminophylline and enprofylline on the protective efficacy of common antiepileptic drugs against electroconvulsions in mice. *Epilepsia* 28: 383-386
94. Cavalheiro EA, Bortolotto ZA, Turski L (1987) Microinjections of the γ -aminobutyrate antagonist, bicuculline methiodide, into the caudate-putamen prevent amygdala-kindled seizures in rats. *Brain Res* 411: 370-372
95. Turski L, Meldrum BS, Turski WA, Watkins JC (1987) Evidence that antagonism at non-NMDA receptors results in anticonvulsant action. *Eur J Pharmacol* 136: 69-73
96. Turski WA, Cavalheiro EA, Coimbra C, Berzaghi MP, Ikonomidou C, Turski L (1987) Only certain antiepileptic drugs prevent seizures induced by pilocarpine. *Brain Res Rev* 12: 281-305
97. Klockgether T, Turski L, Sontag K-H (1987) Towards an understanding of the physiological role of N-methyl-D-aspartate receptors: a more expansive interpretation. *Trends Pharmacol Sci* 8: 20
98. Turski L, Klockgether T, Turski WA, Schwarz M, Sontag K-H (1987) Substantia nigra and motor control in the rat: effect of α -kainate and γ -D-glutamylaminomethylsulphonate on motility. *Brain Res* 424: 37-48
99. Cavalheiro EA, Calderazzo-Filho LS, Bortolotto ZA, Mello L, Turski L (1987) Anticonvulsant role of adenosine. *Pol J Pharmacol Pharm* 39: 537-543
100. Turski L, Cavalheiro EA, Czuczwar SJ, Turski WA, Kleinrok Z (1987) The seizures induced by pilocarpine: Behavioral, electroencephalographic and neuropathological studies in rodents. *Pol J Pharmacol Pharm* 39: 545-555
101. Klockgether T, Schwarz M, Turski L, Sontag K-H (1988) Catalepsy after microinjection of haloperidol into the rat medial prefrontal cortex. *Exp Brain Res* 70: 445-447
102. Schwarz M, Klockgether T, Wüllner U, Turski L, Sontag K-H (1988) δ -Aminovaleric acid antagonizes the pharmacological actions of baclofen in the central nervous system. *Exp Brain Res* 70: 618-626
103. Turski L (1988) Fundamental mechanisms of human brain function - Book review. *Neurochem Int* 12: 247
104. Turski L, Cavalheiro EA, Bortolotto Z, Ikonomidou-Turski C, Kleinrok Z, Turski WA (1988) Dopamine-sensitive anticonvulsant site in the rat striatum. *J Neurosci* 8: 4027-4037
105. Klockgether T, Turski L, Schwarz M, Sontag K-H, Lehmann J (1988) Paradoxical convulsant action of a novel noncompetitive N-methyl-D-aspartate (NMDA) antagonist, tiletamine. *Brain Res* 461: 343-348
106. Ikonomidou-Turski C, Cavalheiro EA, Turski L, Bortolotto ZA, Kleinrok Z, Calderazzo-Filho LS, Turski WA (1988) Differential effects of non-steroidal anti-inflammatory drugs on seizures produced by pilocarpine in rats. *Brain Res* 462: 275-285

107. Turski L, Ikonomidou C, Turski WA, Bortolotto Z, Cavalheiro EA (1989) Review: Cholinergic mechanisms and epileptogenesis. The seizures induced by pilocarpine: A novel experimental model of intractable epilepsy. *Synapse* 3: 154-171
108. Andrews JS, Turski L, Stephens DN (1989) Does the pentylenetetrazole (PTZ) cue reflect PTZ-induced kindling or PTZ-induced anxiogenesis? *Drug Dev Res* 16: 247-256
109. Klockgether T, Schwarz M, Wüllner U, Turski L, Sontag K-H (1989) Myorelaxant effect after intrathecal injection of antispastic drugs in rats. *Neurosci Lett* 97: 221226
110. Turski L, Cavalheiro EA, Calderazzo-Filho LS, Bortolotto Z, Klockgether T, Ikonomidou C, Turski WA (1989) The basal ganglia, the deep prepyriform cortex, and seizure spread: bicuculline is anticonvulsant in the rat striatum. *Proc Natl Acad Sci USA* 86: 1694-1697
111. Cavalheiro EA, Lehmann J, Turski L (1989) Excitatory amino acids - Quo vadis? *Braz J Med Biol Res* 22: 10651067
112. Klockgether T, Turski L (1989) Excitatory amino acids and the basal ganglia: implications for the therapy of Parkinson's disease. *Trends Neurosci* 12: 285-286
113. Turski L, Klockgether T, Turski WA, Schwarz M, Sontag K-H (1990) Entopeduncular nucleus regulates muscle tone in genetically spastic rats: role of substance P and γ -aminobutyric acid. *Brain Res* 509: 347350
114. Turski WA, Cavalheiro EA, Ikonomidou C, Bortolotto ZA, Klockgether T, Turski L (1990) Dopamine control of seizure propagation: Intranigral dopamine D1 agonist SKF-38393 enhances susceptibility to seizures. *Synapse* 5: 113-119
115. Klockgether T, Turski L (1990) Excitatory amino acids and Parkinson's disease. *Trends Neurosci* 13: 46-47
116. Turski L (1990) N-Methyl-D-aspartat-Rezeptorkomplex: Verschiedene Stellen für Regulation und klinische Konsequenzen. *Arzneim.-Forsch./Drug Res* 40: 511514
117. Stephens DN, Schneider HH, Kehr W, Andrews JS, Rettig K-J, Turski L, Schmiechen R, Turner JD, Jensen LH, Petersen EN, Honore T, Bondo Hansen J (1990) Abecarnil, a metabolically stable, anxiolytic β -carboline acting at benzodiazepine receptors. *J Pharmacol exp Ther* 253: 334-343
118. Turski L, Stephens DN, Jensen LH, Petersen EN, Meldrum BS, Patel S, Bondo Hansen J, Löscher W, Schneider HH, Schmiechen R (1990) Anticonvulsant action of the β -carboline abecarnil: Studies in rodents and baboon, *Papio papio*. *J Pharmacol exp Ther* 253: 344-352
119. Wachtel H, Turski L (1990) Glutamate: A new target in schizophrenia? *Trends Pharmacol Sci* 11: 219-220
120. Turski L, Andrews JS, Löscher P-A, Bressler K, Bortolotto ZA, Calderazzo-Filho LS, Cavalheiro EA (1990) Substantia nigra regulates action of antiepileptic drugs. *Brain Res* 520: 232-239

121. Klockgether T, Turski L (1990) Excitatory amino acid antagonists and Parkinson's disease - Reply. *Trends Neurosci* 13: 326-327
122. Turski L, Klockgether T, Schwarz M, Turski WA, Sontag K-H (1990) Substantia nigra: Site of action of muscle relaxant drugs. *Ann Neurol* 28: 341-348
123. Klockgether T, Turski L (1990) NMDA antagonists potentiate antiparkinsonian actions of L-DOPA in monoamine-depleted rats. *Ann Neurol* 28: 539-546
124. Turski L, Niemann W, Stephens DN (1990) Differential effects of antiepileptic drugs and β -carbolines on seizures induced by excitatory amino acids. *Neuroscience* 39: 799-807
125. Turski L, Diedrichs S, Klockgether T, Schwarz M, Turski WA, Sontag K-H, Bortolotto ZA, Calderazzo-Filho LS, Cavalheiro EA (1991) Paradoxical anticonvulsant activity of the γ -aminobutyrate antagonist bicuculline methiodide in the rat striatum. *Synapse* 7: 14-20
126. Turski L, Bressler K, Rettig K-J, Löschmann P-A, Wachtel H (1991) Protection of substantia nigra from MPP⁺ neurotoxicity by N-methyl-D-aspartate antagonists. *Nature* 349: 414-418
127. Löschmann P-A, Lange KW, Kunow M, Rettig K-J, Jahnig P, Honore T, Turski L, Wachtel H, Jenner P, Marsden CD (1991) Synergism of the AMPA-antagonist NBQX and the NMDA-antagonist CPP with L-DOPA in models of Parkinson's disease. *J Neural Transm (P-D Sect)* 3: 203-213
128. Klockgether T, Turski L, Honore T, Zhang Z, Gash DM, Kurlan R, Greenamyre JT (1991) The AMPA receptor antagonist NBQX has antiparkinsonian effects in monoamine-depleted rats and MPTP-treated monkeys. *Ann Neurol* 30: 717-723
129. Cavalheiro EA, Leite JP, Bortolotto ZA, Turski WA, Ikonomidou C, Turski L (1991) Long-term effects of pilocarpine in rats: Structural damage of the brain triggers kindling and spontaneous recurrent seizures. *Epilepsia* 32: 778-782
130. Turski L, Stephens DN (1992) Excitatory amino acid antagonists protect mice against MPP⁺ seizures. *Synapse* 10: 120-125
131. Turski L, Jacobsen P, Honore T, Stephens DN (1992) Relief of experimental spasticity and anxiolytic/anticonvulsant actions of the α -amino-3-hydroxy-5-methyl-4-isoxazoleropionate antagonist 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo(F) quinoxaline. *J Pharmacol exp Ther* 260: 742-747
132. Fink-Jensen A, Judge ME, Bondo Hansen J, Jacobsen P, Turski L, Olney JW, Honore T (1992) Inhibition of cisplatin-induced emesis in ferrets by the non-NMDA receptor antagonists NBQX and CNQX. *Neurosci Lett* 137: 173-177
133. Steppuhn KG, Schneider HH, Turski L, Stephens DN (1993) Long-term treatment with abecarnil does not induce diazepam-like dependence in mice. *J Pharmacol exp Ther* 264: 1395-1400

134. Stephens DN, Turski L (1993) Kindling to the benzodiazepine receptor inverse agonist, FG 7142: Evidence for involvement of NMDA, but not non-NMDA, glutamatergic receptors. *Neuropharmacology* 32: 1011-1017
135. Steppuhn KG, Turski L (1993) Diazepam dependence prevented by glutamate antagonists. *Proc Natl Acad Sci USA* 90: 6889-6893
136. Klockgether T, Turski L (1993) Toward an understanding of the role of glutamate in experimental parkinsonism: Agonist-sensitive sites in the basal ganglia. *Ann Neurol* 34: 585-593
137. Klockgether T, Jacobsen P, Löschmann P-A, Turski L (1993) The antiparkinsonian agent bupirine is an N-methyl-D-aspartate antagonist. *J Neural Transm* 5: 101-106
138. Steppuhn KG, Turski L (1993) Modulation of the seizure threshold for excitatory amino acids in mice by antiepileptic drugs and chemoconvulsants. *J Pharmacol exp Ther* 265: 1063-1070
139. Turski L, Stephens DN (1993) Effect of the β -carboline abecarnil on spinal reflexes in mice and on muscle tone in genetically spastic rats: A comparison with diazepam. *J Pharmacol exp Ther* 267: 1215-1220
140. Turski L, Turski WA (1993) Towards an understanding of the role of glutamate in neurodegenerative disorders: Energy metabolism and neuropathology. *Experientia* 49: 1064-1072
141. Klockgether T, Turski L (1994) Il ruolo del glutammato nel parkinsonismo sperimentale: Siti agonista-sensibili nei gangli basali. *Update Parkinson* 3: 44-45
142. Cavalheiro EA, Fernandes MJ, Turski L, Naffah-Mazzacoratti MG (1994) Spontaneous recurrent seizures in rats: Amino acid and monoamine determination in the hippocampus. *Epilepsia* 35: 1-11
143. Löschmann P-A, Lange KW, Wachtel H, Turski L (1994) MPTP-induced degeneration: Interference with glutamatergic toxicity. *J Neural Transm* 43: 133-143
144. Ikonomidou C, Turski L (1995) Excitotoxicity and neurodegenerative diseases. *Curr Opinion Neurol* 8: 487-497
145. Ikonomidou C, Turski L (1996) Neurodegenerative disorders: Clues from glutamate and energy metabolism. *Crit Rev Neurobiol* 10: 239-263
146. Ikonomidou C, Turski L (1996) Prevention of trauma-induced neurodegeneration in infant and adult rat brain: Glutamate antagonists. *Metab Brain Dis* 11: 125-141
147. Bernert H, Turski L (1996) Traumatic brain damage prevented by the non-N-methyl-D-aspartate antagonist 2,3-dihydroxy-6-nitro-7-sulfamoylbenzo(f)quinoxaline. *Proc Natl Acad Sci USA* 93: 5235-5240

161. Rzeski W, Turski L, Ikonomidou C (2001) Glutamate antagonists limit tumor growth. *Proc Natl Acad Sci USA* 98: 6372-6377
162. Ikonomidou C, Turski L (2002) Why did NMDA receptor antagonists fail clinical trials for stroke and traumatic brain injury? *Lancet Neurology* 1: 383-386
163. Rzeski W, Ikonomidou C, Turski L (2002) Glutamate antagonists limit tumor growth. *Biochem Pharmacol* 64: 1195-200
164. Ikonomidou C, Turski L (2003) Is it time to conclude that NMDA antagonists have failed? *Lancet Neurology* 2: 13
165. Groom AJ, Smith T, Turski L (2003) Multiple sclerosis and glutamate. *Ann N Y Acad Sci* 993: 229-75